Cell Stem Cell
Commentary

Centralized Banks for Human Embryonic Stem Cells: A Worthwhile Challenge

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Centralized banking of human embryonic stem (hES) cells is an endeavor that can benefit individual research efforts and enhance international collaboration but is complicated by the fact that the science is rapidly evolving in an environment of heterogeneous laws, guidelines, and ethical standards. Written from the vantage point of regulatory professionals, this article provides an overview of the benefits of and challenges facing hESC banking enterprises in general with a focus on a global centralized banking effort.

Introduction

Would it not be grand if hESC researchers were able to locate and obtain hESC lines that had clearly documented and approved ethical provenance, that were meticulously characterized, and that met recognized standards for purity, safety, and predictability? This lofty goal has been identified by investigators (Brivanlou et al., 2003) and included in the existing guidelines from the International Society for Stem Cell Research (2007) (ISSCR) and recommendations from other bodies such as the U.S. National Academy of Sciences (2005) (NAS) and the British government.

The ISSCR Guidelines state the following: "Hand in hand with the privilege to perform derivations is the obligation to distribute the cell lines to the research community. A clear, detailed outline for banking and open access to the new lines should be incorporated into derivation proposals. New pluripotent stem cell lines should be made generally available as soon as possible following derivation and first publication. The ISSCR encourages researchers to deposit lines early into centralized repositories where the lines will be held for release and distribution upon publication."

This is a virtual call to action—a call for the creation of centralized repositories or banks. But what exactly is the desired outcome? And, more importantly, what can reasonably be achieved?

Agreement regarding the terms "bank" and "centralized" is a necessary starting point. For the purposes of this document, a bank is an entity that procures, stores, possibly processes, and then distributes materials. The term centralized means "to bring to a center; to concentrate by placing power and authority in a center or central organization" (Webster's Dictionary). In centralized banking, acceptance of centralized control is a key component. It is also important to note that centralized banking may not necessarily refer to a central physical location for the bank (although that might be the case); it may also refer to centralizing the operation, administration, and enforcement of standards for a bank that is physically dispersed.

Implementing these definitions into practice is possible through a variety of designs including (1) a single physical global bank that sets rules and conditions regarding all aspects of hESC acquisition, storage, maintenance, and dispersal; (2) a limited number of regionalized physical banks; or (3) numerous local physical banks. In the model of multiple banks, there must be clear delineation of which centrally based rules of operation and quality control would be mandated, and whether or not regional and local banks would have some degree of autonomy on select issues. Each of these approaches has merit, and each presents distinct logistical challenges.

It has also been suggested that, rather than working toward centralized banks, efforts should focus on the creation of a centralized registry. A registry would provide, in a shareable format, vital information regarding the hESC lines held by different entities. This transparency would seemingly facilitate access to and sharing of hESC lines. In fact, such stem cell registries are being established and are valuable adjuncts to any banking enterprise. The European Human Embryonic Stem Cell Registry was publicly launched in January 2008 (http://hescreg.charite.de/typo3/index.php?id=27). Another registry, part of the International Stem Cell Initiative (ISCI) Project of the International Stem Cell Forum (ISCF, http://www.stemcellforum.org/), is a global stem cell registry of data on approximately 60 hESC lines contributed by 20 laboratories (Andrews, 2007). The ISCI is a global enterprise currently comprising 21 funders of stem cell research sharing the belief that "international collaboration and information sharing will accelerate progress and improve global practice in stem cell research". Registries will also inform the scientific community of the various standards being applied to this research, and this open disclosure may well encourage standardized benchmarking for the derivation and handling of hESCs. But unlike a centralized bank, a registry does not manage the complex logistics of maintaining, propagating, and distributing hESC lines.

The authors acknowledge the value of registries but focus in this article on the goal of establishing a global banking enterprise comprised of a number of national and/or regional hESC banks that aim to provide researchers with quality hESC lines. This goal seems to be in concordance with the international research community, although there is no consensus on exactly what this global enterprise should look like.

The scope of this article is to provide an overview of the benefits and challenges of this vision, and not to present a specific working model of centralized banking or to discuss how to address specific scientific technical details.

This article includes (1) an outline of the general benefits that banking hESC lines offers individual researchers and research institutions, and the specific benefits that centralized banking would offer the global hESC research community; (2) a brief overview of current banking activities and how this could fit into a global banking scenario; and (3) a discussion of the challenges related to establishing hESC banks in general and, more specifically, to a centralized banking effort. While the focus is centralized banking, much of this overview can also inform institutions that are grappling with establishing local repositories.

Why a Bank?

Human embryonic stem cells (hESCs) are pluripotent cells that have the ability to give rise to all of the different cell types in the human body. As such, they present vast potential to provide new insight and new research tools that will hopefully someday support new clinical applications. Excitement over the potential of hESC research has increased the demand for a reliable source of these cells. Investigators have two options: they can derive, validate, expand, and store their own hESC lines or obtain an existing hESC line from another source. The derivation process requires specialized skills and expertise and invites much ethical, regulatory, and legal angst. While some investigators are interested in the derivation process itself, many simply want access to reliable and well-characterized hESC lines. Because hESCs are able to self-propagate, they are a renewable resource that lends itself to sharing. But researchers appropriately demand lines that are scientifically and ethically robust. Investigators need to be assured that the lines they use in their research have been cultured, expanded, and maintained according to most current accepted standards; that the lines meet criteria for determining pluripotency; that they have been screened for purity and safety; and that they were obtained in compliance with appropriate ethical and legal standards.

While an investigator pursuing derivation of hESC lines can clearly make his/her hESCs available to another investigator, such one-to-one transactions have downsides for both the provider and the requestor. Many researchers deriving hESCs are willing to share cell lines but find the process too resource intensive. The person sharing the cells must (1) produce adequate numbers of cells to share; (2) document the authenticity, purity, safety, and stability of the product they are providing; (3) provide documentation of provenance; and (4) deal with any locally required material transfer agreements. These myriad tasks require specialized training, expertise, materials, equipment, and personnel. Many decide that their time, expense, and effort would more productively be applied to the research itself. From the perspective of the requestor, dealing with multiple distinct sources of hESCs requires due diligence with each provider regarding the acceptability of the provenance and biologic quality of each cell line. A bank working as a third party and existing primarily for the purpose of procuring and providing hESCs makes sense for both providers and requestors. A bank can achieve an economy of scale that benefits both parties by providing cell lines that adhere to the highest accepted biologic standards and that have detailed documentation of provenance.

A centralized banking effort, if successful, would be used by the majority of researchers who are deriving hESCs; therefore, the bank would ideally include most of the hESC lines available for sharing. This would increase not only the raw number of lines available for research but also the genetic diversity of available hESC lines by including hESCs that reflect various ethnic groups. In addition, there would be a tremendous benefit to banking hESC lines with disease-associated mutations; for example, lines that have been derived from embryos that have been determined through preimplantation genetic diagnosis (PGD) to have target mutations (Ben-Yosef et al., 2008) or from embryos developed through nuclear transfer (NT) using somatic cells from individuals who have the genetic defect associated with the disease to be studied. (U.S. National Academy of Sciences, 2005).

While the current focus is on research-quality hESCs, the demand for clinical-quality hESCs is rapidly approaching. In fact, some feel that it is here already (Crook et al., 2007). The additional and more stringent regulations for developing and maintaining clinical-level materials, while perhaps daunting for the individual researcher, can more easily be addressed in a centralized system. Prominent researchers (Taylor et al., 2005; Nakajima et al., 2007) have conjectured that banks could ultimately include and make available clinical-grade hLA-typed hESC cells. The benefits of such banks, should they come to pass, could be enormous.

The Current Landscape

The UK Stem Cell Bank (http://www.ukstemcellbank.org.uk/) is clearly the banking leader, with robust and transparent policies to assure the biological quality and ethical sourcing of its cell lines, and an impressive Phase II plan with an international scope to be completed by 2010. The UK bank currently offers the international hESC community access to eight hESC lines and reports that 12 more lines are due for release and 16 additional lines have been ''accessioned.'' However, these 36 lines represent only a fraction of the number of hESC lines that have been derived to date. An overview of stem cell research published in June 2006 (Guhra et al., 2006) found evidence in the literature of 414 existing hESC lines, and there may be many more unpublished lines. Where are these lines, and why is this information unavailable? Does this suggest that researchers are not ''buying in'' to the idea of centralized hESC banking? Or is this a reflection of the limited understanding of and access to centralized banking and/or registries?

A centralized banking enterprise would benefit from international standards for all aspects of hESC derivation, cell culture, and characterization. This goal will be difficult to realize, given the variety of techniques being utilized and the lack of consensus regarding superiority of one practice over others. But there is some progress being made. The ISCF, with 21 international stakeholder members, has created the ISCI project spearheaded by Peter Andrews of the University of Sheffield. Andrews

describes the project: "Our central aim in the initiative is to provide the openness, reliability, and the ability for scientists to reproduce and extend each other's work, which are all crucial to international collaborations between stem cell scientists. This type of initiative is only possible through an organization like the Forum which brings together funders and labs from across the world, all driven by the desire to progress cautiously while benefiting from the huge potential to be derived from working together."

In June 2007, the Initiative published its first milestone—the characterization of 59 hESC lines, including the profiling of 93 different genes (Andrews, 2007). The identified markers can serve as a reliable, common standard to validate hESCs. More than 80 investigators from 17 laboratories in 11 different countries participated in this effort. This bodes well for a "buy in" to the centralized banking enterprise. The Initiative's next project will focus on culture media. Other challenges to be addressed include the following: determination of the most suitable cryopreservation methods for both stable long-term storage and for shipping, and the harmonization of ethics in order to facilitate international transfer of cells. This latter goal of harmonization of ethics is particularly difficult in that it will have to address the vast range of ethical and regulatory approaches being followed in different countries and localities. (For an overview of a new initiative by the ISCF toward the development of an international consensus for hESC banking guidelines, see Healy et al. [2008] in this issue of *Cell Stem Cell*.)

Another group, The Stem Cell Network of the Asia-Pacific (SNAP) region, is a new coalition with representatives from Australia, China, India, Japan, Korea, Singapore, Taiwan, and Thailand that has sited as one of its areas of interest "best practices for cell processes and banking, and methods for culture and differentiation of hES cells" (Sipp, 2007). Members of this regional coalition overlap with those of the ISCI and can help form the framework for a global banking initiative.

The burgeoning number of stem cell journals, stem cell conferences, and stem cell training opportunities point to the collaborative nature of the stem cell community. As much of this attention is focused on sharing advancements in hESC technology, there is cause for optimism that the challenges facing banking are being met head on and the community will indeed buy in to centralized efforts.

Existing hESC Banks

Currently there are a number of operational banks. A brief overview of some of these banks will provide some background to inform how existing banks might or might not fit into a centralized banking framework. A subsequent discussion will detail challenges faced in creating and implementing hESC banking procedures for widespread use in the current international arena.

Public Banks

The UK Stem Cell Bank is the best known and most established repository for hESCs. Although hosted by the UK's National Institute for Biological Standards and Control (NIBSC), a publicly funded scientific organization, the bank aims to be an international resource for all stem cell researchers to deposit and access ethically sourced and well-characterized hESC lines. In addition to the bank's capability to access and distribute "research grade" lines, a great deal of time, care, and money has already been spent to ready the facility to receive and distribute clinical-grade hESC lines that conform to British and U.S. regulatory requirements for transplantation into humans. The bank's policy of transparency makes for easy access to its policies and processes online (Healy et al., 2005).

The United States National Stem Cell Bank has been established by the National Institutes of Health (NIH) and is hosted by WiCell Research Institute, a nonprofit supporting organization of the University of Wisconsin-Madison (http://www.nationalstemcellbank.org/). Its purpose is to acquire, characterize, and globally distribute the 21 hESC lines and their subclones that are listed on the NIH Human Embryonic Stem Cell Registry. Lines listed on the NIH registry are the only hESC lines that can be used in federally funded research in the United States.

Other national and regional stem cell banks have been or are being created in a number of countries including Australia, South Korea, and Spain (Nieto et al., 2006). These banks face hurdles, as evolving regional and national laws make it difficult to formalize operational procedures for their specific banks. For example, Spain's public hESC bank was the subject of lawsuits (since dropped) regarding competing local and national laws governing hESC research activity, which reflected underlying dissonance between the ruling governments in Spain and Andalusia (an autonomous community of Spain) on the ethics of this type of research (Fuchs, 2004). The politicalization of hESC research, not unique to Spain, is a reflection of the controversial nature of this research and a widespread challenge to nations, regions, and localities attempting to establish policies related to in this research.

Public banks, accountable to their constituencies, are well positioned to be regional arms of a global banking enterprise. Nations active in hESC research are currently showing their commitment to international collaboration in a variety of ways, so the growth and cooperation of public banks will be an essential ingredient of a centralized banking enterprise.

Institutional Banks

At the local level, academic research institutions conducting hESC research may house hESC banks to store stem cells derived or acquired by their own institutions. They may have core facilities that process, maintain, store, and distribute hESCs to local investigators. These banks are needed at the local level and can serve as feeders into a physically centralized banking effort.

Commercial Banks

Private industry engaging in stem cell research has its own hESC banks, which may or may not distribute the lines externally. Some examples are the following.

Advanced Cell Technology (ACT, http://www.advancedcell.com/), a biotechnology company that has published peer-reviewed articles on its work, has been working with the U.S. Food and Drug Administration (FDA) in preparation for filing Investigational New Drug (IND) applications to begin clinical trials for the reparation of blood vessels and for the treatment of macular degeneration using hESC-derived cells. ACT has opened two facilities capable of culturing and expanding hESC lines. Each facility has a "master bank" of hESC lines and "working banks" of hESC-derived differentiated stem cells (see ACT).

The StemRide International Limited (SIL) website (http://www.stemride.com/) states that it has a bank of more than 100 hESC lines including 20 lines with genetic or chromosomal abnormalities for distribution to international stem cell researchers. The

company, affiliated with the Reproductive Genetics Institute, an in vitro fertilization (IVF) clinic, provides these lines for a fee. Its website does not provide the transparency of the public stem cell banks, and information on these lines has not been published.

Stem cell banks that are sponsored by the competitive biotechnology industry are naturally proprietary, and industry must carefully consider the pros and cons of participation in a transparent, centralized banking mechanism. Because industry is focused on delivering clinical applications and must work closely with regulatory authorities to do so, commercial companies are uniquely poised to create and support banks of high-quality, clinical-grade hESCs and differentiated cell lines that meet the strictest regulatory requirements.

Operational Challenges of Banking hESC Lines

Determining uniform banking policies and procedures that can foster collaboration is complicated by the fact that the science is rapidly evolving in an environment of heterogeneous laws, guidelines, and ethical standards. The following is a review of some of the challenging operational details that need to be considered. These operational details are relevant to individual freestanding local banks as well as to centralized banks.

Defining the Purpose and Scope of the Bank

It is first necessary to decide what types of cells will be included in the bank. Will the banking be limited to hESCs that are derived from blastocysts? Or will pluripotent cells from alternate sources such as amniotic fluid cells or reprogrammed somatic cells also be included? Will any derivative products (i.e., derived cells) be included as well? Will nonpluripotent stem cells be included? Will the bank include only research-grade cells or also clinical-grade cells? Next, what will be the standards for biological quality, and how will the bank ascertain that banked cells meet those standards? For example, what standard will the bank use to routinely determine pluripotency and purity of the cell line? Because there is no accepted gold standard for many of these determinations, both individual and centralized banks must clearly state and justify what processes will be used and stand ready to modify their procedures in response to new scientific evidence.

A local or a central bank can be narrow or broad in scope. If different types or quality of cells are included, the bank will have to develop a system that segregates the banking activities as a function of cell type and quality. Investigators should expect to request and receive cells that meet specific criteria. The more heterogeneity of materials stored by the bank, the more onerous the recordkeeping and logistics of running the business. A bank with a broad scope may provide a greater resource for investigators but at a higher operations cost. In contrast, a bank with a narrow focus may be more efficiently run but of less value to the broader community.

Determining Ethical Criteria for Banked Cells

The bank must also decide whether or not specific ethical and/or regulatory standards will be imposed on persons depositing hESCs into the bank as well as persons accessing cells from the bank. Both the regulations and the ethics are complicated and open to much local interpretation. Specific ethical issues include, for example, the following: the moral status of the embryo; the use of somatic cell nuclear transfer (SCNT) to derive hESC lines; the interaction with gamete and embryo donors regarding concerns relating to matters such as compensation, consent, privacy; and also some uses of resultant hESCs, especially in terms of chimeras. Recognition of the need to thoughtfully address these issues encouraged the development of guidelines (such as NAS and ISSCR). While the existing guidelines recommend standards, it is important to note that these are voluntary and open to local interpretation and implementation.

In addition to guidelines, there are a variety of country, state, and local laws that directly or indirectly pertain to hESC research. There are new laws written in response to the emergence of this research. There are old abortion and IVF laws that, because of their construct, have an impact on hESC research. Although the regulations and guidelines are a heterogeneous mix, they are consistent in their mandate that materials from which hESCs are derived be procured in an ethical and responsible manner. To that end, most address, for example, recruitment of embryo, gamete, and somatic cell donors and creation of an embryo by fertilization or SCNT for the sole intent of using it for research.

An investigator deriving and/or using hESCs must comply with local law and local interpretation of guidance. Confusion and problems arise when a hESC investigator wants to work with an investigator from another locale that has different laws and/or different interpretation of guidance. While a problem for any collaboration, it is a major problem for banking activities.

It is incumbent on any hESC bank to have transparent policies regarding how the bank will handle the ethical and regulatory aspects of this research. Banks can take different approaches. A bank could assume local laws and guidance interpretations and only accept cells that were derived in compliance with these. A requesting researcher would then have to determine if the bank's standard meets his/her local requirements. This approach is efficient but could limit the availability of cells to requestors operating under similar standards. Or a bank could attempt to develop standards that are consistent with the most protective jurisdictions. Alternatively, a bank could decide to accept lines developed under a variety of standards and categorize hESCs according to specific ethical and regulatory standards of different countries and states. In this scenario, requesting researchers would have the ability to identify and request cells that were in compliance with their own local ethical and legal standards.

It seems that centralized banks would be more inclined to implement the last approach. This does not mean that a centralized bank would be obligated to accept "any and all" cells: the bank would likely identify some nonnegotiable requirements, thus establishing a common denominator for the content of the bank (but with more flexibility than option two); for example, requiring that the derivation of deposited cell lines was approved by an ethical review board or a stem cell research oversight (SCRO) process as suggested by the ISSCR guidelines ensuring the absence of coercion in the procurement process, identifying elements that must be included in consent forms, etc.

At the present time, most hESC lines are considered "anonymous" in that they have no identifiers and no link back to specific donors. This may change for several reasons, including, for example, the emergence of clinical-grade hESCs with consideration of traceability of the tissue donor(s), and also the increasing use of PGD embryos, which may simply be difficult to anonymize. The inclusion of any "identifiable" cell lines in a bank will require processes for protecting the confidentiality of donors. In addition, if relevant, consent forms will have to include the

fact that personal information will be linked to resultant hESC lines. Carefully navigating issues related to the privacy of the information stored in hESC banks will be critical to ensuring public trust in the banking enterprise.

While defining any ethical and regulatory floor will be a prodigious undertaking, once the floor has been determined, banks must also develop processes for implementation. An example of an ethical decision that has significant implementation issues is how much control, if any, donors should have regarding the fate of the hESC lines that were derived from their tissue (Holm, 2005). There are two basic questions. First, would the bank accept hESCs that were derived from embryos or other material if the persons donating the material stipulated in their consent form that they wanted to be able to direct the use of resultant lines to specific types of research? If such hESCs would be accepted, the bank would need a mechanism to deliver on this promise. The second issue is the ability to withdraw from the research. If donated materials were anonymized prior to hESC derivation, withdrawal of hESCs would be logistically impossible. But, if a particular hESC line remains linked to the identity of a donor or donors, and the donor(s) withdraws consent, what will happen to any resulting hESC line? The bank could decide that any resultant hESCs will be destroyed—or, conversely, the bank could decide that withdrawal applies only to the donated materials and not to resultant hESC lines. In either case, the bank should proactively develop policies to address these unlikely but difficult situations.

Handling Procured Materials

One of the main benefits of centralized hESC banking is to remove from investigators the burdens of propagating adequate numbers of hESCs as well as maintaining and routinely evaluating the inventory for quality. Therefore, most hESC banks will have to address the technical challenges related to all aspects of cell culture, expansion, scale-up processes for widespread distribution, and storage. The enormity of this task cannot be stressed enough (Stacey and Auerbach, 2007). It is important to note that in order for a particular hESC line to maintain its integrity, it must be maintained, stored, and expanded under certain conditions so that they do not lose their initially defined characteristics that are seen in the earliest passages. Does the bank have the skill to dissect and recover cells from the original cell line? What processes will be put in place to "manufacture" batches of consistently identical cells hESCs over time? How will they assure microbiological safety? What quality assurance steps will be implemented? What validation assays will be used?

And these technological aspects of hESC research are rapidly evolving: how will the bank identify and accommodate the most current standards? For example, as cryopreservation protocols are re-examined and improved to increase survival rate of high-quality hESCs that do not easily differentiate or otherwise change their characteristics upon thaw (Hunt, 2007), how will the bank have the resources to assure that the most effective techniques are being employed?

Although the authors write from the perspective of nonscientists, the challenges involved in establishing best banking practices in an evolving field are well appreciated. Those establishing banks would benefit from consulting the "experts" and putting in mechanisms to course correct as standards advance. Hopefully, the future will bring improvements in hESC culture techniques, allowing an element of stability and predictability.

Determining Criteria for Accession and Responsibilities of the Requestor

The bank must have rules regarding who can access hESCs from the bank. The bank could provide specimens to anyone who asks, or it could develop eligibility criteria relating to the requestor and/or proposed use of the cells. Requirements for requestors could include, for example, only providing cells to an investigator at an institution that has an oversight process for hESC research, such as an embryonic stem cell oversight committee (ESCRO). Another criterion could be that the requestors provide documentation of expertise in handling hESCs or even other cells in culture. But what standard should be used to assess these criteria? And is it realistic for a bank to assume the responsibility of policing these criteria? Will the bank have any different process for investigators from academia versus industry versus a government agency? Will the bank ask for verification that the proposed research is legal in the country and/or state in which it will be conducted? Will the bank ask for a formal documentation of local approval? Or will a promissory note from the investigator suffice? Presumably, ultimate liability for the legality of any use of hESCs received from a bank would lie with the requestor of the cells and the individuals actually performing the research or using the cells. However, the bank providing the materials must establish clear parameters regarding any internal screening and/or approval of a requestor's proposed uses that the bank will perform before releasing the cells. Banks should consider to what extent their internal review and oversight of proposed uses could increase their potential liability. As any bank is developed, it would be helpful to meet with local ethical oversight committees to determine which, if any, actions of the bank would need formal committee approval. The relevant committees would be the ethical review committee, such as an institutional review board (IRB), and the hESC oversight committee, such as an ESCRO or SCRO.

Will the bank have a contract with the requestor requiring that relevant results of any research be returned to the bank? If research provides information regarding the character of a particular cell line, this could be very helpful to the bank in terms of labeling the cell line for future requestors. The return of research results to tissue repositories is becoming the standard for some non-hESC banks, such as the new NIH-supported Genome-Wide Association Studies (GWAS) (U.S. Department of Health and Human Services, http://grants.nih.gov/grants/gwas/index.htm). But such an arrangement may not be reasonable to the hESC researchers themselves. This raises issues of claims to intellectual property (IP). If a discovery is made from a specific cell line, who has IP rights to the discovery? The person who did the subsequent research? The deriver of the hESCs? The bank itself? These rules must be known up front to allow the person deriving the cells to make an informed decision about whether or not to use the services of the bank.

Business Questions

It costs money to run any bank, and the depositors as well as the recipients should expect to pay for this service. The associated costs will differ tremendously as a function of the involvement of the bank. For example, a bank that independently characterizes and/or manipulates the hESCs will have higher costs. There are a number of ways to cover the costs. Obviously, one solution would be to obtain outside funding from foundations,

universities, or state or federal coffers. Requestors of hESCs will likely be asked to pay a fee for obtaining the hESCs: will this be to cover costs of that specific transaction? Or more? Will depositors receive anything for providing their cells to the bank? Or will depositors be expected to pay for having their cells managed by the bank? Thought will need to be given to any local rules prohibiting payment in exchange for human tissue (to the extent they apply to hESC lines); these types of restrictions are fairly common but often contain exceptions for reasonable administrative costs related to the transaction at issue. The bank must also consider the investment that it makes to any particular cell line, by maintaining them in culture, intermittently assessing their biologic status, and possibly generating more hESCs from the original line. A bank that invests this amount of time and effort may also expect exclusivity from the depositors and have them promise that she or he will use only this one bank as the banking source for a specific cell line.

The rules of any bank will be determined to some degree by who owns or controls the bank. The obvious options include academia, industry, private foundation/organization, or a government agency. There are benefits and challenges associated with each of these. The cost of such an enterprise may require government ownership, but government involvement may invoke certain requirements or limitations onto banking procedures and policies that might not otherwise apply under private ownership. For example, in the United States, the current restriction on federal funding of research involving hESC lines created after August 9, 2001, limits the content of a government-supported national bank considerably. If controlled by private industry, the issues of IP and potentially conflict of interest increase. And if controlled by an academic entity, there is the question of resources. And there is the concern that the bank could be overly influenced by that academic center's hESC researchers. It would be important to have banking operations be distinct from the goals and interests of local researchers. Ownership by a private foundation/organization is attractive in that it may facilitate neutrality and buy in, but the concern of both immediate and long-term resources is not trivial.

Conclusion

Despite the numerous challenges to the creation of hESC banks, any challenges are far outweighed by the potential benefits. There are many reasons for supporting centralized hESC banks that can serve an international clientele. hESC research is a global enterprise that begins at the local level. The resources needed to further this research should be available to researchers throughout the world. Centralized banks capitalize on the reality of economy of scale; the resources and expertise required for maintaining and characterizing these cells are substantial. Maintaining and routinely evaluating these cells for quality requires an investment of space, equipment, and personnel. Centralizing these efforts at a single (or a few) site(s) is responsible use of these resources. The availability of hESCs to many investigators would thus be maximized and would potentially focus the research on the use of the hESCs themselves rather than the derivation process or the validation and expansion processes.

While the scientific and ethical/legal standards of banked materials raise a number of questions, comprehensive and transparent banking activities help to inform the discussion and create the necessary community to forge reasonable standards. A large centralized hESC banking enterprise would serve a central role in the creation of uniform ethical and scientific standards, minimize the continuing emergence of local interpretations and standards, and ultimately enhance collaboration, increasing the output of this new area of research. Whether or not the many jurisdictions that oversee hESC banks will be able to harmonize their technical and ethical standards remains to be seen; however, it is indeed a worthy goal.

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